

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

REC'D 18 APR 2006

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PCT

## PCT

### WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:  
ALAN J. GRANT  
CARELLA, BYRNE, GILFILLAN, CECCHI, STEWART &  
OLSTEIN  
5 BECKER FARM ROAD  
ROSELAND, NJ 07068

Date of mailing  
(day/month/year)

13 APR 2006

Applicant's or agent's file reference

689290.213

**FOR FURTHER ACTION**

See paragraph 2 below

International application No.

PCT/US04/33072

International filing date (day/month/year)

07 October 2004 (07.10.2004)

Priority date (day/month/year)

08 October 2003 (08.10.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC: C12Q 1/68( 2006.01); C07H 21/04( 2006.01)

USPC: 435/6;536/22.1

Applicant

AVALON PHARMACEUTICALS, INC

**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Date of completion of this opinion

17 February 2006 (17.02.2006)

Authorized officer

Valerie Belt-Harris  
Gary Benzion

Telephone No. (571) 272-1600

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/33072

**Box No. I Basis of this opinion**

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
- ☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing
- ☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper
- ☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.
- ☐ filed together with the international application in electronic form.
- ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/33072

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 3-43

because:

☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require an international search (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for said claims Nos. 3-43

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13<sup>ter</sup>.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/US04/33072

**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims <u>none</u>	YES
	Claims <u>1-2</u>	NO
Inventive step (IS)	Claims <u>none</u>	YES
	Claims <u>1-2</u>	NO
Industrial applicability (IA)	Claims <u>1-2</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-2 lack novelty under PCT Article 33(2) as being anticipated by Sakakura et al. (Int. J. Cancer, 2000, Vol. 89, pg. 217-223).

Sakakura et al. disclose the limitations of the claims (See pg. 217, the abstract).

Claims 1-2 lack an inventive step under PCT Article 33(3) as being obvious over Sakakura et al. (Int. J. Cancer, 2000, Vol. 89, pg. 217-223).

It would have been prima facie obvious to apply the method of Sakakura et al. for identifying a cancer-target gene and the target gene is useful as a marker for prognosis.

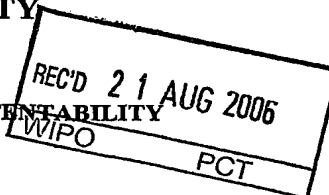
Claims 1-2 meet the criteria set out in PCT Article 33(4), and thus the instant invention has industrial applicability because the subject matter claimed can be made or used in industry for identifying a cancer target-gene and the target-gene is useful as a marker for identifying cancers.

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 689290.213	<b>FOR FURTHER ACTION</b>	See Form PCT/IPEA/416
International application No. PCT/US04/33072	International filing date (day/month/year) 07 October 2004 (07.10.2004)	Priority date (day/month/year) 08 October 2003 (08.10.2003)
International Patent Classification (IPC) or national classification and IPC IPC: C12Q 1/68( 2006.01);C07H 21/04( 2006.01) USPC: 435/6;536/22.1		
Applicant AVALON PHARMACEUTICALS, INC		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
  - a. ☐ (sent to the applicant and to the International Bureau) a total of \_\_\_ sheets, as follows:
    - ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
    - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
  - b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) \_\_\_\_\_, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:
 

<input checked="" type="checkbox"/>	Box No. I	Basis of the report
<input type="checkbox"/>	Box No. II	Priority
<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/>	Box No. IV	Lack of unity of invention
<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/>	Box No. VI	Certain documents cited
<input type="checkbox"/>	Box No. VII	Certain defects in the international application
<input type="checkbox"/>	Box No. VIII	Certain observations on the international application

Date of submission of the demand 05 May 2005 (05.05.2005)	Date of completion of this report 06 August 2006 (06.08.2006)
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer <i>Valerie Bell-Harris</i> Joyce Tung Telephone No. (571) 272-1600

Form PCT/IPEA/409 (cover sheet)(April 2005)

# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/US04/33072

## Box No. I Basis of the report

1. With regard to the language, this report is based on:

- ☒ the international application in the language in which it was filed.
- ☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
- ☐ publication of the international application (under Rule 12.4(a))
- ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☐ the international application as originally filed/furnished
- ☒ the description:  
 pages 1-56 as originally filed/furnished  
 pages\* NONE received by this Authority on \_\_\_\_\_  
 pages\* NONE received by this Authority on \_\_\_\_\_
- ☒ the claims:  
 pages 57-63 as originally filed/furnished  
 pages\* NONE as amended (together with any statement) under Article 19  
 pages\* NONE received by this Authority on \_\_\_\_\_  
 pages\* NONE received by this Authority on \_\_\_\_\_
- ☒ the drawings:  
 pages NONE as originally filed/furnished  
 pages\* NONE received by this Authority on \_\_\_\_\_  
 pages\* NONE received by this Authority on \_\_\_\_\_
- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/US04/33072

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 3-43

because:

☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for said claims Nos. 3-43

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.  
PCT/US04/33072**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>1 and 2</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-2</u>	NO
Industrial Applicability (IA)	Claims <u>1-2</u>	YES
	Claims <u>NONE</u>	NO

**2. Citations and Explanations (Rule 70.7)**

Claims 1-2 lack novelty under PCT Article 33(2) as being anticipated by Sakakura et al. (Int. J. Cancer, 2000, Vol. 89, pg. 217-223). Sakakura et al. disclose the limitations of the claims (See pg. 217, the abstract).

Claims 1-2 lack an inventive step under PCT Article 33(3) as being obvious over Sakakura et al. (Int. J. Cancer, 2000, Vol. 89, pg. 217-223).

It would have been prima facie obvious to apply the method of Sakakura et al. for identifying a cancer-target gene and the target gene is useful as a marker for prognosis.

Claims 1-2 meet the criteria set out in PCT Article 33(4), and thus the instant invention has industrial applicability because the subject matter claimed can be made or used in industry for identifying a cancer target-gene and the target-gene is useful as a marker for identifying cancers.



# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/33072

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC: C12Q 1/68( 2006.01);C07H 21/04( 2006.01)  USPC: 435/6;536/22.1 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/6; 536/22.1  Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched none  Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,Y	KETTUNE et al. Gene Expression Profiling of Malignant Mesothelioma Cell Lines: cDNA Array Study, Int. J. Cancer, 2001, Vol. 91, pg. 492-496. see the abstract.	1-2
X,Y	ISOLA et al. Genetic Alterations in ERBB2-amplified Breast Carcinomas, Clinical Cancer Research, 1999, Vol. 5, pg. 4140-4145. see the abstract.	1-2
X & Y	SAKAKURA et al. Amplification and Over-Expression of the AIB1 Nuclear Receptor C0-Activator Gene in Primary Gastric Cancers, 2000, Vol. 89, pg. 217-223. see the abstract.	1-2
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	
Date of the actual completion of the international search 17 February 2006 (17.02.2006)		Date of mailing of the international search report 13 APR 2006
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201		Authorized officer Gary Benzion Telephone No. (571) 272-1600

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/33072

## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  2. ☒ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
  3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
- Remark on Protest**
- |                          |   |
|--------------------------|---|
| <input type="checkbox"/> | The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.   |
| <input type="checkbox"/> | The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation. |
| <input type="checkbox"/> | No protest accompanied the payment of additional search fees.   |

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US04/33072

### BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-2, drawn to a method for identifying a cancer-target gene and a set of cancer-target gene.

Group II, claim(s) 3-9, drawn to a method for identifying an agent that modulates the activity of a cancer-target gene.

Group III, claim(s) 10-17, and 19 drawn to a method for identifying an agent an anti-neoplastic agent.

Group IV, claim(s), 18 drawn to a method for determining the cancerous status of a cell.

Group V, claim(s) 20-23, drawn to a method for identifying an agent that modulates the activity of a cancer-target polypeptide.

Group VI, claim(s) 24-30, drawn to an antibody.

Group VII, claim(s) 31-41, drawn to a method for treating cancer.

Group VIII, claim(s) 42, drawn to a cancer target gene identified in Table 6.

Group IX, claim(s) 43, drawn to a method for producing test data with respect to the gene modulating activity of a compound.

The inventions listed as Groups I-IX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group I is for identifying a cancer-target gene and a set of cancer-target gene, Group II is for identifying an agent that modulates the activity of a cancer-target gene, Group III is for identifying an agent an anti-neoplastic agent, Group IV is for determining the cancerous status of a cell, Group V is for identifying an agent that modulates the activity of a cancer-target polypeptide, Group VI is drawn to an antibody, Group VII is for treating cancer, Group VIII is drawn to a cancer target gene identified in Table 6 and Group IX is for producing test data with respect to the gene modulating activity of a compound. Based upon the limitations of each group, they lack the same or corresponding special technical features.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US04/33072

Continuation of B. FIELDS SEARCHED Item 3:  
WEST AND STN  
MEDLINE, CAPLUS, BIOSIS, EMBASE